24. (New) A method according to Claim 23, in which phosphorylation at Thr-495 is detected.

REMARKS

I. Nationalization

This application represents the U.S. national stage of International Patent Application PCT/AU99/00968, filed November 05, 1999, which claims priority to Australian Patent Application PP 6976, filed November 06, 1998.

As the text of the International Application was transmitted by the International Bureau, an additional copy is not required to satisfy 35 U.S.C. § 371(c)(2). Nonetheless, for the Examiner's convenience, a copy of international application PCT/AU99/00968 is enclosed in the form of the published PCT Application WO 00/28076.

As there are no "substitute pages" within the written text, and after consultation with Australian counsel, Applicants' representative confirms that the text of the enclosed published PCT application corresponds to the text of the international application as filed. As the substitute pages of drawings were entered at the appropriate time during PCT examination, they will have been transmitted to the U.S. Office by the International Bureau.

Should formal amendments be necessary to conform to U.S. practice, Applicants seek to introduce such amendments into the present specification by, *e.g.*, deleting the PCT cover page, providing the Abstract as a separate page, and deleting the PCT header.

Priority is also properly claimed by an amendment at page 1.

II. National Stage Claims

After according a U.S. filing date, and **before** calculating the filing fee, entry of the foregoing claim amendments is respectfully requested. The changes to the pending claims are being made solely to conform to U.S. practice. New claims are being entered, beginning with claim 14. The new claims are fully supported by the PCT and priority application. None of the revised or new claims constitute new matter. The submission of revised claims does not represent abandonment of any of the subject matter of the claims in the international application.

III. Status of the Claims

At the conclusion of the PCT examination phase, claims 1-13 were pending (see IPER as well as PCT publication, both enclosed). The IPER finds each of claims 1-13 to have unity of invention, and is completely favorable regarding the novelty, inventive step and industrial applicability of all claims.

Presently, claims 5, 6, 8-10, 12 and 13 have been amended to render them singly dependent. No claims have been canceled. Claims 14-24 have been added, which are fully supported by the original specification.

Claims 1-24 are therefore in the case. For the convenience of the Examiner, a copy of the pending claims showing the revisions is included herewith as **Exhibit A**. A clean copy of the pending claims is included herewith as **Exhibit B**.

IV. Support for the Claims

Aside from removing the multiple dependencies in claims 5, 6, 8-10, 12 and 13, no changes to the pending claims have been introduced. Claims 1-13 thus represent those at the conclusion of PCT examination essentially in unamended form.

New claims 14-24 are supported throughout the specification. For example, exemplary support for claims 14-21 is particularly prominent at page 16, with exemplary support for claims 22-24 being prominent at page 17 and in the supporting figures. See also, page 4, lines 25-27, concerning the use of antibodies to phosphorylated at Ser-1177, confirming that this site is phosphorylated during ischemia.

Claims 17 and 18 are supported by the sequences in the original specification, although CRIRTQSpFSLQER reflects the addition of C at the N-terminus and GITRKKTpFKEVANC reflects deletion of V at the C-terminus. Those of ordinary skill in the art would understand the CRIRTQSpFSLQER sequence to properly reflect the addition of a cysteine at the N-terminus as cysteine is known in the art to be used for coupling peptides to keyhole limpet haemocyanin, described in the specification as being used in antibody generation. In terms of GITRKKTpFKEVANC, the deletion of valine from the C-terminus reflects the peptide actually used in immunization. Those of ordinary skill in the art would, in light of the present disclosure, understand the valine in question to be V504 of the primary eNOS sequence, and would therefore understand that the presence or absence of this valine would not be material to the generation of antibodies with specificity for the phosphorylated peptide as opposed to the dephosphorylated peptide. This is because the valine at position 504 is sufficiently removed from the threonine residue that becomes phosphorylated, *i.e.*, the threonine at position 495.

It will therefore be understood that no new matter is encompassed by any of the amended or newly presented claims.

V. Compliance with 37 C.F.R. § 1.121

Copies of the pending claims are attached hereto as **Exhibit A** and **Exhibit B**. In accordance with 37 C.F.R. § 1.121, the claims have been labeled as "(Amended") or "(New)", where appropriate. **Exhibit A** provides a clean copy of the pending claims, whereas **Exhibit B** shows the changes with brackets and underlining.

The proper claim for priority has been timely introduced into the specification by amendment of the opening paragraph at page 1. A 199 word Abstract is also introduced into the specification by amendment as a separate page.

The amendments to the opening paragraph at page 1 of the specification and the abstract have been made as "Replacement Sections" in accordance with 37 C.F.R. §§ 1.121(b)(2), 1.77(b)(2) and 1.77(b)(10). This is proper under 37 C.F.R. §§ 1.121(b)(2)(i)(ii)(iii), as the specification contains section headings as provided in 37 C.F.R. § 1.77, and the amendments include the reference, replacement section in clean form and another version of the replacement section separate from the amendment marked up to show all changes (**Exhibit C**).

VI. Fees and Formalities

The national filing fee and claim fees are included herewith. The fees have been calculated **after** the present changes to remove the multiple dependencies in the claims. Any omitted fees should be deducted from Williams, Morgan & Amerson Deposit Account No. 50-0786/4050.000900.

Applicants are entitled to small entity status. An executed declaration to this effect is no longer required.

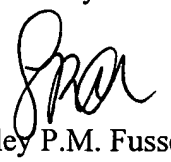
VII. Conclusion

The IPER issued for the international application finds all claims to have unity of invention. Applicants therefore urge that they define a unified invention for the purposes of examination in the U.S.

Importantly, the IPER also holds that all claims meet the requirements for industrial applicability, novelty and inventive step. This is compelling evidence that the present claims have utility and define a novel and non-obvious invention that should be progressed to allowance in the United States.

In light of the positive IPER, Applicants submit that the present case is in condition for allowance and such favorable action is respectfully requested. Should the Examiner have any questions or comments, a telephone call to the undersigned Applicants' representative is earnestly solicited.

Respectfully submitted,



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